Complete Summary

GUIDELINE TITLE

Stem cell transplant for acute lymphocytic/lymphoblastic leukemia (adult).

BIBLIOGRAPHIC SOURCE(S)

Stem cell transplant for acute lymphocytic/lymphoblastic leukemia (adult). Philadelphia (PA): Intracorp; 2005. Various p. [47 references]

GUIDELINE STATUS

This is the current release of the guideline.

All Intracorp guidelines are reviewed annually and updated as necessary, but no less frequently than every 2 years. This guideline is effective from April 1, 2005 to April 1, 2007.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acute lymphocytic leukemia (ALL), also called acute lymphoblastic leukemia and acute lymphoid leukemia

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Oncology

INTENDED USERS

Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Utilization Management

GUIDELINE OBJECTIVE(S)

To present recommendations for stem cell transplantation for acute lymphocytic/lymphoblastic leukemia that will assist medical management leaders to make appropriate benefit coverage determinations

TARGET POPULATION

Adult patients with acute lymphocytic/lymphoblastic leukemia

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Pre-procedure patient assessment including:
    - All current medication, recent laboratory tests, serologies, ABO blood type, human leukocyte antigen typing, recent electrocardiogram and x-ray, mammogram for females over 40 years of age, prostate specific antigen screening in males over 45 years of age, colonoscopy, psychosocial evaluation
2. Additional information (gastrointestinal, vascular, pulmonary, neurological, dental)

Management/Treatment

1. Hematopoietic stem-cell transplantation
    - Allogeneic transplantation
    - Autologous transplantation

Note: Non-myeloablative allogeneic stem-cell transplantation for adult acute lymphocytic/lymphoblastic leukemia is considered experimental, investigational, or unproven and is not recommended.

MAJOR OUTCOMES CONSIDERED

- Rate of treatment-related mortality and a two-year overall survival in patients who received non-myeloablative conditioning

- Overall and disease-free survival rates in patients receiving allogeneic or autologous hematopoietic stem cell (HSC) transplant
- Complications of HSC transplantation

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: reviews by independent medical technology assessment vendors (such as the Cochrane Library, HAYES); PubMed; MD Consult; the Centers for Disease Control and Prevention (CDC); the U.S. Food and Drug Administration (FDA); professional society position statements and recommended guidelines; peer reviewed medical and technology publications and journals; medical journals by specialty; National Library of Medicine; Agency for Healthcare Research and Quality; Centers for Medicare and Medicaid Services; and Federal and State Jurisdictional mandates.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A draft Clinical Resource Tool (CRT or guideline) is prepared by a primary researcher and presented to the Medical Technology Assessment Committee or the Intracorp Guideline Quality Committee, dependent upon guideline product type.

The Medical Technology Assessment Committee is the governing body for the assessment of emerging and evolving technology. This Committee is comprised of a Medical Technology Assessment Medical Director, the Benefit and Coverage Medical Director, CIGNA Pharmacy, physicians from across the enterprise, the Clinical Resource Unit staff, Legal Department, Operations, and Quality. The Intracorp Guideline Quality Committee is similarly staffed by Senior and Associate Disability Medical Directors.

Revisions are suggested and considered. A vote is taken for acceptance or denial of the CRT.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Approval Criteria

Stem cell transplant for acute lymphocytic/lymphoblastic leukemia (ALL) (adult) may be approved for the following indications provided that no contraindications are present: (see "Contraindications" field)

Therapeutic

Allogeneic hematopoietic stem-cell (HSC) transplantation for the treatment of acute lymphocytic/lymphoblastic leukemia when the following medical necessity criteria are met:

- Availability of a human leukocyte antigen (HLA)-matched donor (at least five of six HLA-match) AND any ONE of the following:
    - Failed induction therapy
    - First remission for patients with poor prognosis*
    - Second or subsequent remission

Autologous HSC transplantation for the treatment of acute lymphocytic/lymphoblastic leukemia when the following medical necessity criteria are met:

- Not eligible for allogeneic stem-cell transplantation AND
- First remission for patients with poor prognosis* OR
- Second remission

Non-myeloablative allogeneic HSC transplantation for adult acute lymphocytic/lymphoblastic leukemia is considered experimental, investigational, or unproven.

*Poor-prognosis adult acute lymphocytic/lymphoblastic leukemia includes ANY of the following:

- Longer than four weeks to achieve a complete remission
- Age over 35 years
- White blood cell count (WBC) greater than 30 x 10^9/L in B-lineage ALL
- WBC greater than 100 x 10^9/L in T-cell lineage ALL
- Null cell phenotype
- Extramedullary disease
- Presence of chromosome abnormalities t(9;22)(q34;q11) (the Philadelphia chromosome), t(4;11), t(8,14), t(2,8), and t(8,22)
- Elevated B2-microglobulin
- Deletion of chromosome 7
- Trisomy 8

Controversial Indications

May not be supported by scientific evidence - Physician advisor review suggested.

Therapeutic

- The following information should be requested on all patients:
    - Recent clinical summary including all current medication and treatment plans
    - Recent labs (complete blood count [CBC], differential, blood urea nitrogen [BUN], electrolytes, creatinine clearance, platelets, profiles: lipid, liver, renal, coagulation)
    - Serologies: human immunodeficiency virus (HIV); hepatitis A, B, C; cytomegalovirus (CMV); Epstein-Barr (EBV); herpes (HSV); varicella (VZV)
    - Purified Protein Derivative (PPD) testing for tuberculosis (with history of exposure, past history, or family history of tuberculosis). High-risk recipients (Asians, past history of drug abuse) should also be tested.

- ABO blood type, human leukocyte antigen (HLA) typing
- Recent electrocardiogram (EKG) and chest x-ray
- Results of gynecologic (GYN) exam with Papanicolaou (Pap) smear within the past year for females 18 or older
- Mammogram for females over 40
- Prostate specific antigen (PSA) screening in all adult males over 45 years of age
- Stools for guaiac x 3. Colonoscopy for patients over 50 years of age or at an earlier age if positive stool guaiac
- Psychosocial evaluation performed at transplant center

- Additional information may be indicated as listed below:
  - Gastrointestinal (GI)
    - GI screening for all patients with positive guaiac stools, history of polyps, or previous GI bleed: esophogastroduodenoscopy (EGD) or colonoscopy
    - Flexible sigmoidoscopy or barium enema (BE) if >45 years old
    - Gallbladder ultrasound for patients with history of cholelithiasis
  - Vascular
    - Carotid Doppler studies on all patients with a history of transient ischemia attacks (TIAs), cardiovascular accident (CVA), and for all patients who have carotid bruits
    - Lower extremity Doppler studies on all patients with a history of peripheral vascular disease (PVD), diabetes, and for those patients who have abnormal peripheral pulses on examination
  - Pulmonary
    - Pulmonary function tests (PFTs) for those patients with a history of airway disease
  - Other consults/evaluations
    - Neurology
    - Dental

Contraindications

Physician advisor review is suggested.

See "Contraindications" field for absolute and relative contraindications to HSC transplantation.

Complications

See "Potential Harms" field for potential complications of stem cell transplant for acute lymphocytic/lymphoblastic leukemia.

The original guideline document provides a list of red flags that may affect disability duration and relevant return-to-work tables.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

General Potential Benefits

Appropriate use of hematopoietic stem cell transplantation in adult patients with acute lymphocytic/lymphoblastic leukemia

Specific Benefits

- The conditioning regimen for autologous transplantation is less toxic than the one for allogeneic hematopoietic stem cells (HSC) transplantation and does not create a graft-versus-host reaction.
- Potential advantages of umbilical-cord blood transplant (UCBT) over marrow or blood stem-cell transplants include:
    - Large potential donor pool
    - Rapid availability, since the cord blood has been prescreened, tested and frozen and is ready to use
    - No donor attrition, since the UCB stem cells are already stored
    - No risk or discomfort for the donor
    - Low incidence of contamination by viruses
    - Lower risk of graft-versus-host disease (GVHD), even for recipients with a less-than-perfect tissue match

Groups Most Likely to Benefit

- Patients who failed induction therapy
- Patients in first remission at high risk for relapse
- Patients in second or subsequent remission

POTENTIAL HARMS

Potential Complications in Bone Marrow Transplant Patients

- Temporary and common side effects include hair loss, nausea, vomiting, fatigue, oral ulcers, and skin reaction.
- Infections: patients are at serious risk of developing infections in the several months after transplant. Cytomegalovirus, Aspergillus, and Pneumocystis are among the most common causes of serious infections, including pneumonia.
- Graft-versus-host disease (GVHD) is one of the most serious and life-threatening complications. Symptoms of this may develop within days or as

long as 3 years after transplantation. Acute GVHD usually occurs within six months. Chronic GVHD develops after 6 months
- Bleeding, especially in the first month after transplant. Platelet or red blood cell (RBC) transfusions may be required.
- Organ complications may include liver disease, renal failure, pneumonitis and pulmonary fibrosis, and cardiotoxicity.
- Graft failure or graft rejection

Long-term Complications

- Infertility
- Menstrual irregularities
- Sterility
- Growth problems in children
- Cataracts
- Secondary cancers

CONTRAINDICATIONS

CONTRAINDICATIONS

Absolute contraindications to hematopoietic stem-cell (HSC) transplantation include (but are not limited to):

- Active central nervous system involvement
- Presence of any significant co-morbid medical or psychiatric illness which would significantly compromise the patient's clinical care and chances of survival
- Advanced age (allogeneic only)
- Active disease (autologous only)

Relative contraindications to HSC transplantation include (but are not limited to):

- Poor cardiac function (ejection fraction <45%)
- Poor liver function (bilirubin >2.0mg/dL and transaminases greater than two times normal), unless related to acute lymphocytic leukemia (ALL)
- Poor renal function (creatinine clearance <50 ml/min)
- Poor pulmonary function (diffusion capacity [DLCO] <60% of predicted)
- Presence of human immunodeficiency virus (HIV) OR the active form of ANY of the following:
    - Hepatitis B
    - Hepatitis C
    - Human T-cell lymphotropic virus type 1 (HTLV-1)
- Karnofsky rating <60% and/or Eastern Cooperative Oncology Group (ECOG) performance status 2 (refer to the original guideline document for details on Karnofsky rating)

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Stem cell transplant for acute lymphocytic/lymphoblastic leukemia (adult). Philadelphia (PA): Intracorp; 2005. Various p. [47 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 (revised 2005)

GUIDELINE DEVELOPER(S)

Intracorp - Public For Profit Organization

SOURCE(S) OF FUNDING

Intracorp

GUIDELINE COMMITTEE

CIGNA Clinical Resources Unit (CRU)
Intracorp Disability Clinical Advisory Team (DCAT)
Medical Technology Assessment Committee (MTAC)
Intracorp Guideline Quality Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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Reprints of complete guideline content may be purchased for $35.00 per title (plus tax in TX at 8.25% and CT at 1.0%). Please send e-mail request to lbowman@mail.intracorp.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Policies and procedures. Medical Technology Assessment Committee Review Process. Philadelphia (PA): Intracorp; 2004. 4 p.
- Online guideline user trial. Register for Claims Toolbox access at www.intracorp.com.

Licensing information and pricing: Available from Intracorp, 1601 Chestnut Street, TL-09C, Philadelphia, PA 19192; e-mail: lbowman@mail.intracorp.com.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 24, 2005. The information was verified by the guideline developer on June 7, 2005.

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